

INTERNATIONAL SEARCH REPORT

International Application No.

EP 03/07399

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C07K16/18 A61K39/395 A61K38/00 A61K31/00
 A61K48/00 C12Q1/68 G01N33/53 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

MEDLINE, BIOSIS, EPO-Internal, PAJ, WPI Data, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 95/28484 A (AMGEN INC) 26 October 1995 (1995-10-26)</p> <p>page 11, line 9-12 page 13, line 29-33 figure 1 table 2 claims 1,31,33</p> <p style="text-align: center;">--- -/-</p>	<p>28, 29, 31, 33, 34, 36, 51, 53</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
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- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

28 June 2004

Date of mailing of the international search report

13. 07. 2004

Name and mailing address of the ISA

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Y	<p>ZOU JUNE X ET AL: "An Eph receptor regulates integrin activity through R-Ras" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 96, no. 24, 23 November 1999 (1999-11-23), pages 13813-13818, XP002265365 Nov. 23, 1999 ISSN: 0027-8424 page 13818</p> <p>-& KIYOKAWA ETSUKO ET AL: "Overexpression of ERK, an EPH family receptor protein tyrosine kinase, in various human tumors" CANCER RESEARCH ISSN: 0008-5472, vol. 54, no. 14, 1994, pages 3645-3650, XP001156923 abstract page 3647, right-hand column, line 3</p>	1-4, 6-12,15, 28-31, 33-36, 51,53
Y	<p>VOGT THOMAS ET AL: "Eph-receptor tyrosine kinase profiles of malignant melanomas at a glance: cDNA miniarray discloses expression profiles indicative for redundant autocrine loops" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, no. 41, March 2000 (2000-03), page 788 XP001156950 91st Annual Meeting of the American Association for Cancer Research.; San Francisco, California, USA; April 01-05, 2000, March, 2000 ISSN: 0197-016X abstract</p>	1-4, 6-12,15, 28-31, 33-36, 51,53
Y	<p>KATAOKA HIDEKI ET AL: "Expression profile of EFNB1, EFNB2, two ligands of EPHB2 in human gastric cancer" JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, vol. 128, no. 7, July 2002 (2002-07), pages 343-348, XP001156841 ISSN: 0171-5216 abstract page 344, left-hand column, paragraph 1 page 345, right-hand column, last paragraph page 347, right-hand column, paragraphs 3,4</p>	1-4, 6-12,15, 28-31, 33-36, 51,53

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Y	HOLDER NIGEL ET AL: "Eph receptors and ephrins: Effectors of morphogenesis" DEVELOPMENT (CAMBRIDGE), vol. 126, no. 10, May 1999 (1999-05), pages 2033-2044, XP001156919 ISSN: 0950-1991 abstract page 2039, left-hand column, paragraph 3 -right-hand column, paragraph 1	1-4, 6-12,15, 28-31, 33-36, 51,53
A	OVING IRMA M ET AL: "Molecular causes of colon cancer." EUROPEAN JOURNAL OF CLINICAL INVESTIGATION. ENGLAND JUN 2002, vol. 32, no. 6, June 2002 (2002-06), pages 448-457, XP002265366 ISSN: 0014-2972 the whole document	1-4, 6-12,15, 28-31, 33-36, 51,53
A	HERZIG M ET AL: "Recent advances in cancer research: mouse models of tumorigenesis" BBA - REVIEWS ON CANCER, ELSEVIER SCIENCE BV, AMSTERDAM, NL, vol. 1602, no. 2, 21 June 2002 (2002-06-21), pages 97-113, XP004356804 ISSN: 0304-419X page 100, left-hand column, last paragraph -right-hand column, paragraph 1	1-4, 6-12,15, 28-31, 33-36, 51,53
A	MARIADASON J M ET AL: "Down-regulation of beta-catenin TCF signaling is linked to colonic epithelial cell differentiation." CANCER RESEARCH. UNITED STATES 15 APR 2001, vol. 61, no. 8, 15 April 2001 (2001-04-15), pages 3465-3471, XP002223972 ISSN: 0008-5472 the whole document	1-4, 6-12,15, 28-31, 33-36, 51,53
A	NAISHIRO Y ET AL: "Restoration of epithelial cell polarity in a colorectal cancer cell line by suppression of beta-catenin/T-cell factor 4-mediated gene transactivation." CANCER RESEARCH. UNITED STATES 15 MAR 2001, vol. 61, no. 6, 15 March 2001 (2001-03-15), pages 2751-2758, XP002223973 ISSN: 0008-5472 the whole document	1-4, 6-12,15, 28-31, 33-36, 51,53

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A	<p>HARADA N ET AL: "Introduction of antisense CD44S CDNA down-regulates expression of overall CD44 isoforms and inhibits tumor growth and metastasis in highly metastatic colon carcinoma cells." INTERNATIONAL JOURNAL OF CANCER. JOURNAL INTERNATIONAL DU CANCER. UNITED STATES 1 JAN 2001, vol. 91, no. 1, 1 January 2001 (2001-01-01), pages 67-75, XP002223971 ISSN: 0020-7136</p> <p>-& WIELENGA-VJ ET AL.: "Expression of CD44 in Apc and Tcf mutant mice implies regulation by the WNT pathway" AMERICAN JOURNAL OF PATHOLOGY, vol. 154, no. 2, February 1999 (1999-02), page 515-23 XP002224014</p>	
X	<p>WO 01/98350 A (CHIRON CORP) 27 December 2001 (2001-12-27)</p> <p>abstract claims 1-23</p>	<p>1-4,6-9, 15,21, 27-31, 33-36, 42,48,51</p>
A	<p>WO 00/70076 A (HUMAN GENOME SCIENCES INC ;NI JIAN (US); ROSEN CRAIG A (US); FAN P) 23 November 2000 (2000-11-23)</p> <p>abstract paragraph '0004!; table 1 page 82-84 page 106 page 138 page 153, last paragraph page 165, line 16,17</p>	<p>1-4,6-9, 11,12, 15,20, 26, 28-31, 33-36, 41,47,51</p>

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X	<p>WO 02/051438 A (MAX PLANCK GESELLSCHAFT ;STAHL BERND (DE); MACCHI PAOLO (DE); BONH) 4 July 2002 (2002-07-04)</p> <p>abstract page 5, paragraph 2 page 6, paragraphs 1,3 page 9, paragraph 4 page 10, paragraphs 1,2 page 11, paragraph 2 page 13, paragraphs 2-4 page 14, paragraphs 1,4,5 page 15, paragraph 2 page 16, paragraph 3 page 17, paragraph 4 page 19, paragraphs 2,3</p>	<p>1-4,6-9, 15,20, 26, 28-31, 33-36, 41,47,51</p>
X	<p>WO 00/73801 A (OBATA YUICHI ;LUDWIG INST CANCER RES (US)) 7 December 2000 (2000-12-07)</p> <p>abstract page 6, line 17-27 page 11, line 21-31 page 12, line 12-17 page 23, paragraphs 8-32 page 29, line 21 page 34, line 23 -page 35, paragraph 1 page 44, line 10-25 page 52, line 29-32</p>	<p>1-9,15, 20,26, 28-36, 41,47,51</p>
X	<p>WO 99/48921 A (ORGANON NV ;SPEK PETRUS JOHANNES V D (NL); UNIV LELAND STANFORD JU) 30 September 1999 (1999-09-30)</p> <p>abstract claims 1-18</p>	<p>28,29, 31,33, 34,36, 38,44, 51,53</p>
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E	<p>US 2003/235910 A1 (MONIA BRETT P ET AL) 25 December 2003 (2003-12-25) abstract</p>	<p>1</p>

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X	WO 02/00939 A (DIADEXUS INC ; MACINA ROBERTO A (US); PILLAI RAJESWARI (US)) 3 January 2002 (2002-01-03) abstract page 35, line 32-35 page 37, last paragraph -page 40, paragraph 1 page 55, last paragraph page 68, paragraph 2 page 82, line 33-35	1,2,4-7, 9,11,15, 19,28, 29, 31-36, 40,46, 51,53
P,X	WO 02/084294 A (AXXIMA PHARMACEUTICALS AG ;HERGET THOMAS (DE); COTTEN MATTHEW (DE)) 24 October 2002 (2002-10-24) claims 1-29	1,2,4-7, 15,19, 25,51
Y	MOERK H ET AL: "INVERSE MRNA EXPRESSION OF THE SELENOCYSTEINE-CONTAINING PROTEINS GI-GPX AND SEP IN COLORECTAL ADENOMAS COMPARED WITH ADJACENT NORMAL MUCOSA" NUTRITION AND CANCER, LONDON, GB, vol. 37, no. 1, 2000, pages 108-116, XP008014221 ISSN: 0163-5581 abstract page 108, left-hand column page 109, left-hand column, paragraphs 1,2. page 110, right-hand column, paragraph 3 page 112, right-hand column -page 113, left-hand column page 114, left-hand column, paragraph 2 -right-hand column, paragraph 1 -/-	1,2,4, 6-12,15, 19,25, 28,29, 31, 33-36, 40,46, 51,53

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Y	FLORIAN S ET AL: "Cellular and subcellular localization of gastrointestinal glutathione peroxidase in normal and malignant human intestinal tissue." FREE RADICAL RESEARCH. SWITZERLAND DEC 2001, vol. 35, no. 6, December 2001 (2001-12), pages 655-663, XP009032640 ISSN: 1071-5762 the whole document	1,2,4, 6-12,15, 19,25, 28,29, 31, 33-36, 40,46, 51,53
A	KELNER M J ET AL: "Structural organization of the human gastrointestinal glutathione peroxidase (GPX2) promoter and 3'-nontranscribed region: transcriptional response to exogenous redox agents" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 248, no. 1-2, May 2000 (2000-05), pages 109-116, XP004198802 ISSN: 0378-1119 the whole document	1,2,4, 6-12,15, 19,25, 28,29, 31, 33-36, 40,46, 51,53

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